Surveillance for Sporadic Foodborne Disease in the 21st Century: The FoodNet Perspective

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THE CHALLENGE OF FOODBORNE DISEASES SURVEILLANCE IN THE UNITED STATES

How safe is our food? Can it be made safer? In the United States alone, foodborne infections have been estimated to cause ∼76 million illnesses, 325,000 hospitalizations, and 5000 deaths each year [1]. The annual cost of foodborne illnesses caused by the 4 most common bacterial pathogens alone (*Salmonella* strains, *Shigella* and *Campylobacter* species, and *Escherichia coli*) has been estimated at $6.9 billion [2]. Measuring improvements in the safety of the nation's food supply is, therefore, a challenging but critical public health priority [3].

Although changes in regulation, education, and technology have dramatically improved the safety of our food supply since the early 20th century, attaining further reductions in the incidence of foodborne illness will pose more complicated challenges. Mass production and distribution and importation of food have benefited consumers in several ways. More varieties of fruits and vegetables are now available in local supermarkets, and many are sold year-round. Nevertheless, these gains are not without costs. Importation of produce into the United States can introduce new pathogens to a susceptible population. The industrialization of the food supply, which helps make food inexpensive and plentiful, has also enabled pathogens to spread through the population rapidly and more broadly than might have occurred when food was produced and distributed more locally. In addition, new pathogens have emerged and come to the consumer in an increasing variety of food vehicles [4]. For example, *Campylobacter* species and *E. coli* O157:H7 were first recognized as common causes of foodborne illness in the early 1980s. The importance of the caliciviruses and of the parasitic pathogen *Cyclospora* is still unfolding. In 1982, >200 pathogens that cause acute illnesses were known to be transmitted through food [5]. Today, many more pathogens could be added to the list, and it is likely that still more remain to be identified. Thus, to reduce the burden of illness from foodborne diseases, new problems must be identified and quantified.

National laboratory-based surveillance for some infections, such as salmonellosis, has long been used to drive prevention efforts. In 1962, clinical laboratories that isolated *Salmonella* strains from humans began to send isolates to their state public health laboratories for serotyping, who in turn mailed the results to the Centers for Disease Control and Prevention (CDC; Atlanta, GA). These serotyping data helped to unravel the epidemiology of salmonellosis. Today, serotype-specific data are reported electronically to the CDC, and a new generation of subtyping methods based on PFGE has been introduced for routine subtyping of *E. coli* O157, *Salmonella,* and other pathogens [6]. This surveillance can help rapidly identify and investigate outbreaks. However, similar national surveillance strategies have not been available for other foodborne pathogens, such as *Campylobacter* species, because of limited methods and resources.

Creating effective national surveillance for an emerging pathogen depends on developing new clinical and laboratory practices and changing policies in many jurisdictions; it can be a slow process. In 1995, reliable nationwide surveillance was not available for *Campylobacter, Vibrio,* or *Yersinia* infections or for any of the parasitic foodborne infections. Surveillance for *Listeria* infections was available through an active sentinel surveillance network for invasive bacterial infections [7]. This network provided the infrastructure for conducting population-based surveillance for an array of such pathogens, with the flexibility to add more as new diagnostic strategies came into use in clinical laboratories. Moreover, it could provide a platform for detailed description and investigation of sporadic cases of infection. Sporadic infections—those cases not clearly linked to an outbreak—are far more common but are much less likely to be investigated than

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are cases associated with recognized outbreaks.

For some years, CDC epidemiologists proposed that an active sentinel surveillance system for foodborne diseases be established, but funding was not available. Then, between November 1992 and February 1993, a large outbreak of *E. coli* O157 infection in several western states caused >700 infections and resulted in 4 deaths [8]. Illnesses were traced to thousands of pounds of contaminated hamburger patties that were undercooked at many outlets of one fast-food restaurant chain. This outbreak focused public and regulatory attention on the need to reduce the number of pathogenic organisms in meat. As a result of the heightened concern, the Food Safety and Inspection Service (FSIS) of the US Department of Agriculture (USDA) developed more comprehensive regulations under the Pathogen Reduction, Hazard Analysis and Critical Control Point Program (HACCP) System final rule [9].

These regulations, which began to be implemented in 1997, provide for systematic reduction of pathogen contamination during slaughter and subsequent processing, verified with expanded microbiologic testing of meat and meat products. Would this extensive overhaul of the country's meat inspection system have any impact on human illness? In 1995, the FSIS of the USDA and the CDC began to explore how an enhanced surveillance system might answer the question. With support from the FSIS and the US Food and Drug Administration (FDA) and as a result of increasing public concern, funds were made available through the National Food Safety Initiative to establish an enhanced sentinel surveillance system for foodborne illness.

IMPACT OF THE FOODBORNE DISEASES ACTIVE SURVEILLANCE NETWORK (FOODNET)

Established in 1996, FoodNet is a collaborative effort by the Emerging Infections Program of the CDC, the USDA/FSIS, the FDA, and now 9 state health departments (those of California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, and Tennessee). FoodNet conducts active surveillance for 7 bacterial and 2 parasitic diseases that are often foodborne within a defined population. The goals of FoodNet are to determine more precisely the frequency and severity of foodborne diseases that occur in the United States, to monitor trends in specific foodborne diseases, and to determine the proportion of foodborne disease attributable to specific foods.

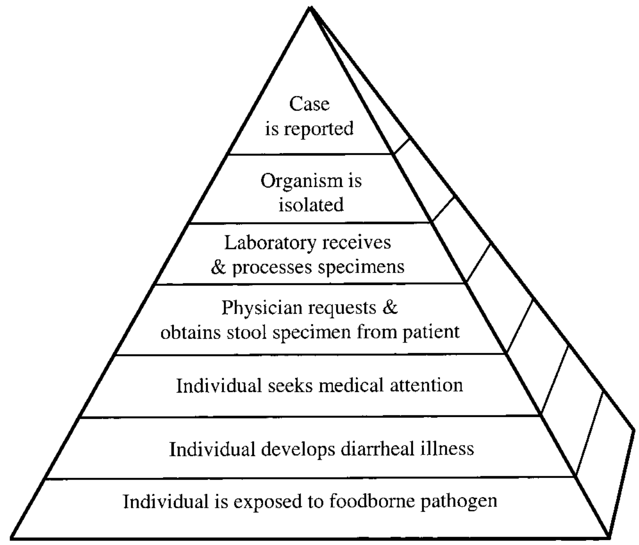

Figure 1. The "burden of illness pyramid" used by FoodNet to assess the burden of foodborne disease in the United States.

The establishment of FoodNet represented a turning point in foodborne disease surveillance for 3 reasons. First, before the inception of FoodNet, there were no precise estimates of the burden of foodborne illness in the United States. Policymakers and regulatory agencies, when faced with allocating limited resources, had difficulty assessing the burden of foodborne illness. FoodNet provided a more rigorous scientific method in this area by adopting a paradigm known as the "burden of illness pyramid" (figure 1). This paradigm considers the chain of events that must occur for an episode of illness in the general population to be registered in surveillance. Any break in the chain of events leads to the illness not being recorded in national surveillance. FoodNet estimates the proportion of cases that are unrecognized at each level of this pyramid by conducting surveys of the general population [10, 11], by querying clinicians regarding their clinical practices [12], and by surveying clinical laboratories to assess testing methodologies [13]. For example, the study by Voetsch et al. [14] in this supplement estimates the burden of nontyphoidal *Salmonella* infections in the United States. Telephone surveys were done in 5 FoodNet surveillance areas (also known as "FoodNet sites") to determine the proportion of persons with diarrheal illness who sought medical care and the proportion for whom stool samples were submitted for bacterial culture. In addition, all 264 clinical microbiology laboratories in FoodNet sites were surveyed regarding practices for testing of stool specimens; laboratory records were regularly audited to ensure complete reporting of *Salmonella* isolates. Voetsch et al. [14] conclude that 38.6 cases of *Salmonella* infection occurred for each culture-confirmed case reported.

The second reason that FoodNet has had a significant impact on food safety is that the establishment of accurate and timely surveillance is integral to the cycle of public health prevention and the control of foodborne illness (figure 2). From 1996 to 2002, there has been a documented downward trend in the incidence of infections caused by *Campylobacter, Listeria,* and *Yersinia* species and *Salmonella* serotype Typhimurium (figure 3) [15]. These decreases occurred in the context of a number of changes in the food safety system, including the implementation of new meat and poultry regulations, efforts to reduce the prevalence of some pathogens on farms, and improvements in food handling practices in restaurants. The decline in the incidence of infections caused by *S.* Typhimurium coincided with a decline in the prevalence of *Salmonella* isolation from FSIS-regulated products to levels below those at baseline, before the HACCP was established [16]. In contrast, after an initial decline, the incidence of infections caused by *Salmonella* serotype Enteritidis did not change significantly between 1996 and 2002 [15]. Implementation of nationwide, mandatory, preventive control measures on farms throughout the country would reduce the risk for human illness from *S.* Enteritidis–contaminated eggs; such control measures have been followed by decreases in *S.* Enteritidis infection in some regions where they have been implemented [17]. Thus, rigorous surveillance can serve as the basis for assessing the effectiveness of public health interventions.

The third reason for FoodNet's impact is that the network serves as a platform for the conduct of special studies that could not be completed otherwise. The FoodNet infrastructure has been used to conduct 17 case-control studies of sporadic foodborne disease, including investigations of infection with fluoroquinolone-resistant *Campylobacter* species [18, 19], *E. coli* O157:H7 [20], and *Salmonella* strains [21–25]. FoodNet also was used to conduct a rapid search for cases of variant Creutzfeldt-Jakob disease when that issue

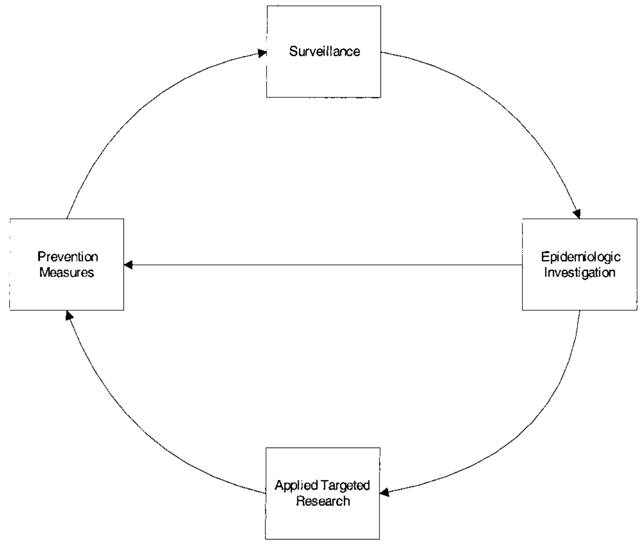

Figure 2. The role of surveillance in the cycle of public health prevention and control of foodborne illness.

emerged in 1996, and, reassuringly, no cases were found [26]. In the future, other special studies of emerging infections can be undertaken as well.

Seven years of FoodNet surveillance have now been completed. Since 1996, FoodNet has provided data on some infections that are often foodborne—including *Campylobacter, E. coli* O157:H7, *Listeria, Yersinia,* and *Vibrio* infections—but for which reliable national surveillance data were not otherwise available. In 1997, surveillance for *Cyclospora* and *Cryptosporidia* infections was added, to begin tracking these important parasitic infections. FoodNet depends on the ability of clinical laboratories to identify infections, and, because the diagnosis of infection due to non-O157, Shiga toxin–producing strains of *E. coli* has improved recently, infection with these organisms has been included in FoodNet surveillance. Active surveillance for pediatric cases of hemolytic uremic syndrome (through a network of pediatric nephrologists) was also added in 1997.

A SURVEY OF THIS SUPPLEMENT

In this *Clinical Infectious Diseases* supplement, a variety of articles present assessments of the stability and sources of geographic variation in the incidence of foodborne infections and examine trends over time. Several articles focus on limitations in the quality of data used to estimate the incidence of foodborne illnesses. For example, Jones et al. [27] note in their study of foodborne outbreaks that, in 71% of outbreaks, no confirmed etiology was found and, in 45%, the suspected food vehicle could not be identified. They rightly conclude that, without adequate resources for epidemiologic investigation and collection and testing of clinical samples, the factors that contribute to these outbreaks will not be understood. Other factors limit the ability to characterize the burden of foodborne disease. For example, Hennessey et al. [12] show that physicians do not order stool cultures and other important stool studies with optimal frequency. Furthermore, even when physicians routinely send stool specimens to the laboratory for culture, they frequently do not order tests for ova and parasites, as explained in the article by Jones et al. [28]. The burden of disease caused by parasites such as *Cryptosporidia, Cyclospora, Microsporidia,* and *Toxoplasma* is thus difficult to quantify.

Many of the studies in this supplement

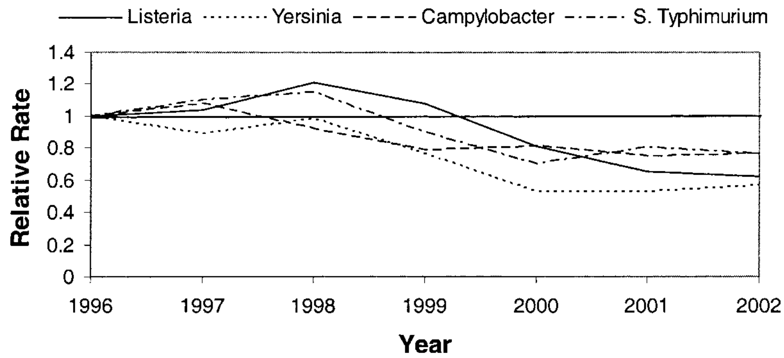

Figure 3. Relative rates of infections caused by *Salmonella* serotype Typhimurium and *Campylobacter, Listeria,* and *Yersinia* species in FoodNet sites, 1996–2002.

relate to the burden of disease caused by *Salmonella* infection and the associated risk factors. Chicken consumption in the United States was not previously associated with *S.* Enteritidis infections, but consumption of chicken prepared outside the home was a major risk factor detected in the study of sporadic *S.* Enteritidis infections by Kimura et al. [23]. This suggests that additional control measures, beyond those focused on eggs, may be relevant to prevention of this infection. In another article, by Hennessey et al. [24], we learn that eating eggs outside the home is an important risk factor for developing gastroenteritis caused by *Salmonella* serotype Heidelberg. *S.* Heidelberg is the now the fourth most common *Salmonella* serotype reported in the United States, and it accounted for 6% of all *Salmonella* infections in 2001 [29]. Not all *Salmonella* infections are foodborne, as we are reminded in the article on reptile- and amphibian-associated *Salmonella* infections by Mermin et al. [21]. It is surprising that, among persons <21 years of age, reptile or amphibian exposure has an even greater attributable risk for *Salmonella* infections than does eating eggs in restaurants or traveling outside the United States.

Two articles describing the epidemiology of sporadic *E. coli* O157:H7 infections are included in this supplement. Bender et al. [30] reveal that the incidence of this infection initially increased and then declined during the period 1996–1999. No definite trend was discernible. They also suggest that some of the differences in incidence between states might be accounted for by different physician and laboratory practices. Kassenborg et al. [20] studied sporadic *E. coli* O157:H7 infection and found that eating undercooked hamburgers and exposure to cattle on farms are important risk factors. Perhaps this should come as no surprise, given the well-established association between these infections and consumption of contaminated ground beef. However, in this study, only eating hamburgers at table-service restaurants was linked with infection; eating hamburgers at fast food (i.e. non–table service) restaurants was not. Kassenborg et al. [20] speculate that USDA guidelines implemented in 1994 that prohibited the sale of ground beef known to be contaminated with *E. coli* O157:H7 might have impacted the level of risk associated with eating hamburgers at fast-food restaurants. It may also reflect changes in hamburger cooking practices in that segment of the food-service industry.

The news of *Campylobacter* is mixed. *Campylobacter* species are a frequent cause of bacterial gastroenteritis in the United States. The good news, according to Samuel et al. [31], is that the incidence is decreasing, especially in California. But bad news is presented as well. As with *Salmonella,* antimicrobial resistance among *Campylobacter* strains is emerging as a concern in the United States and many other industrialized nations. In a study of fluoroquinolone-resistant *Campylobacter* infection by Kassenborg et al. [19], 2 important risk factors emerged—travel outside the United States and eating turkey or chicken prepared at a commercial establishment. Because poultry is a major food reservoir for *Campylobacter,* and because the principal identified route of domestically acquired fluoroquinolone-resistant *Campylobacter* infection is through poultry, the authors conclude that a serious look at the use of fluoroquinolones in poultry is warranted.

FUTURE DIRECTIONS

The articles presented in this supplemental issue represent just a sample of the types of investigations made possible through FoodNet. The potential for future useful studies through FoodNet is great. FoodNet could be used to identify and investigate pathogens not currently under surveillance. An extended panel of laboratory tests is now being used in collaborating laboratories in 2 FoodNet sites to investigate cases of acute diarrheal episodes of undetermined etiology, and, in the future, these tests could help identify new pathogens. FoodNet also might provide an important platform for investigation and analysis of new and emerging foodborne pathogens so that the best surveillance and prevention mechanisms can be developed.

FoodNet data eliminate the effect of

variations in the states' reporting requirements and enable more-substantive data analyses of other sources of variation. The reasons that *Campylobacter* infection is more common in California, *E. coli* O157 infection more common in Minnesota and Oregon, *S.* Enteritidis infection more common in the Northeast, and *Yersinia* infection more common in Georgia may be assessed by examining possible geographic differences in risk factors (in case-control studies) or geographic differences in the frequency of exposure (in population survey data).

Similarly, the National Antimicrobial Resistance Monitoring System for Enteric Bacteria now measures the prevalence of resistance to a standard panel of antimicrobial agents in a sample of strains of *Salmonella, Campylobacter, E. coli* O157:H7, and other bacteria obtained in FoodNet sites and other geographical areas [32]. Integrating these data with the clinical and epidemiological data on those same infections collected through FoodNet can help define the clinical impact of resistance and the association of resistant infections with specific exposures. Comparison of the data from FoodNet with data from other databases can provide greater insight into the epidemiology of foodborne infections and into progress in preventing them. In particular, the spectrum of subtypes of a pathogen isolated from humans can be compared with the spectrum of subtypes of the same pathogen isolated from several animal reservoirs. This may be of great value in the future if specific subtypes (for example, specific PFGE-identified types within a single serotype of *Salmonella*) are associated with a single reservoir.

The mass production and distribution of food makes it difficult to detect multistate outbreaks that may be related to low-level contamination of food. Other mechanisms have been implemented that enable the linking of seemingly sporadic infections to a common source. For example, national surveillance for 4 major foodborne pathogens—*Salmonella* strains, *Listeria* and *Shigella* species, and *E. coli* 0157—now exists in all 50 states. In most of these states, clinical laboratories routinely submit isolates to the state public health laboratories for serotyping and/or molecular subtyping. Supported by the Food Safety Initiative, a national molecular subtyping system called PulseNet was established in 1996 by the CDC and state health departments. Under PulseNet, which now includes 50 states and several local health departments as well as the food safety laboratories of the FDA and the FSIS, all 4 major foodborne pathogens are subtyped and compared electronically [6]. Subtyping systems, such as PFGE for *E. coli* O157 and *Listeria* species, provide fingerprints for each bacterial isolate. Identical fingerprints from bacterial strains isolated in different regions of the country should improve the rapidity and precision with which outbreaks and outlying cases are detected and improve our ability to link certain subtypes to specific food sources. National surveillance combined with powerful new typing systems (now becoming routine in many state public health laboratories) enables the recognition of these previously camouflaged "connections" between far-flung cases of infection. Future potential applications of FoodNet include incorporating many of the gains in surveillance provided by PulseNet.

The cycle of public health prevention begins with the critical first step: surveillance. FoodNet can help develop better surveillance methods, identify populations at risk, define areas in need of further investigation, and define the success of prevention measures that are implemented. The results of the investigations and analyses made possible by FoodNet are expanding not only our knowledge of how foodborne illness is transmitted but also its impact on human health. As a result of these surveillance efforts, new ideas and investigations are likely to lead to improved prevention strategies and a safer food supply.

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